## REMARKS

### A. Introduction

The undersigned attorney wishes to thank Examiner Deborah Davis for her comments in a telephone interview on December 16, 2003. Since the Amendment After Final was not entered in parent application Serial No. 09/804,774, filed on March 13, 2001, the undersigned attorney discussed with Examiner Deborah Davis the following:'

1. Filing a continuation application reasserting the claims as asserted in the Amendment After Final; and
2. Including an Affidavit pointing out how the Grow reference does not apply.

At the same time, the original application would be abandoned in favor of the continuation application.

Examiner Davis indicated she agreed with this course of action and, if convinced of the arguments concerning the Grow reference, would allow the continuation application.

### B. Status of the Claims

Claims 1-4, 6, and 8-21 are pending in the application.

Claims 5 and 7 have been withdrawn from consideration.

With this amendment, independent Claims 1 and 15, and dependent Claim 9 have been amended.

## C. Background of the Invention

Currently, approximately 15,000 new compounds are invented per year. Of the 15,000 compounds invented per year, only one or two are found to be suitable drugs for clinical trials. A clinical trial may cost a hundred million dollars to conduct. Therefore, it becomes extremely important to quickly and economically determine which of the approximately 15,000 compounds invented per year has the best potential to be further evaluated. Also, the efficacy of the particular compound must be quickly evaluated. It is important for this to be done even prior to conducting animal studies on the compound of interest. This would save millions of dollars in the evaluation of a particular compound prior to formal pre-clinical studies.

This invention is aimed at reducing time and expense and to provide a cost effective way to evaluate these potential compounds to determine which compounds are to go to animal experiments or clinical trials. Particularly important is to determine which compounds are efficacious at the cellular level.

## D. Current Invention

The current invention is directed towards the use of direct Raman imaging, not Raman spectroscopy, to determine the absorption and distribution of a compound within living cells . This determination is made by use of direct Raman imaging. Because direct Raman imaging is being used, not dot mapping spectroscopy, the time to acquire the compound absorption and distribution is much less. Therefore, the cells remain viable and alive during the experiment.

## E. Grow Reference Does Not Apply

The primary reference used by the Examiner rejecting all of the claims of the present application is U.S. Patent No. 5,866,430 to Grow. As was explained to Examiner Davis and her supervisor during the in-person interview on October 28, 2003, the Grow reference does not apply. The Grow reference uses a method of bio-concentration to increase sensitivity of the Raman spectrum, not direct Raman imaging. Direct Raman imaging is not used to determine drug action in a living cell. The only Raman imaging referenced in Grow is to detect the bio-concentrator. The Grow reference is a portable bio-sensor device using Raman spectroscopy. Raman imaging is mentioned in Grow as one of many ways of detecting a bio-concentrated mixture, not drug uptake in a living cell. The Grow reference relies to a large extent upon binding interactions in a bio-concentrate.

As is pointed out in the Joint Affidavit of Dr. Jian Ling and Michael A. Miller, the Grow reference only mentions Raman imaging as a way of detecting the bio-concentrated mixture. The casual mention of "imaging" in Grow is simply used to detect the bio-concentrated mixture. Even the referenced claims of Grow (Claims 5 and 15) have a bio-concentrator in independent Claim 1, from which both claims depend.

As was specifically pointed out in the interview, Grow utilizes a Raman spectrum. The current invention selects a peak or frequency band in the Raman spectrum and then uses only that band to obtain direct a Raman image of a drug under investigation in a living cell, not

Raman spectrum of the same. The Grow reference deals with analyte identification, concentration and (in some cases) quantitation using Raman spectroscopy, but not direct Raman imaging of a drug distribution within living cells.

The Sharonov reference demonstrates the use of fluorescence imaging to determine distribution of anti-tumor drugs within living cancer cells, not the use of direct Raman imaging. It is important to state that fluorescence and Raman imaging are based upon two fundamentally different and independent physical processes, which can be delineated by the field of quantum mechanics. Fluorescence is a process in which electrons are promoted to an excited electronic state and then decay radiatively to an electronic state of lower energy than the excited state, whereas Raman is a process in which photons are scattered by means of exciting electrons to, and returning from, virtual states with net energy difference equivalent to a vibrational state. In addition, Sharonov does not disclose the various steps as contained in either independent Claim 1 or independent Claim 15. There is no "processing," dividing," or "comparing" to determine drug distribution within living cells as is specifically claimed.

## CONCLUSION

There is a tremendous need in the industry for this type of simple, inexpensive method to evaluate the efficacy of a particular potential drug. The Grow reference deals with Raman spectroscopy, not direct Raman imaging, and particularly not the direct Raman imaging of drug action within living cells.

Claim 1, as amended, claims a direct Raman image at a predetermined wavelength on

said Raman spectrum. It is a comparison of the direct Raman images that determines drug efficacy. This is also claimed in independent Claim 15. The difference between independent Claim 1 and independent Claim 15 is that Claim 1 claims a particular method of comparing the Raman images, whereas Claim 15 claims the comparing in a broader context.

For the reasons given hereinabove, Applicants respectfully submit the claims are now proper in form and substance. A Notice of Allowance is respectfully solicited.

Respectfully submitted,

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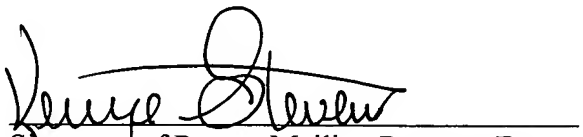

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